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INTERFERENCE WITH *COXIELLA BURNETII* INFECTIONS OF GUINEA PIGS BY INFLUENZA A VIRUS

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ABSTRACT

Guinea pigs exposed by the respiratory route to sublethal doses of influenza virus, PR8 strain, resisted subsequent challenge with a lethal dose of Coxiella burnetii administered by the same route. This note describes this interference phenomenon.

INTERFERENCE WITH COXIELLA BURNETII INFECTIONS OF GUINEA PIGS BY INFLUENZA A VIRUS

Guinea pigs* exposed by the respiratory route to sublethal doses of influenza virus, PR8 strain, resisted subsequent challenge with a lethal dose of Coxiella burnetii administered by the same route. This note describes this interference phenomenon.

Materials and methods used in the aerosol exposure of guinea pigs to influenza virus were described previously.[1] Influenza virus suspensions with titers of $10^{9.4}$ to $10^{9.8}$ median egg infectious dose per ml (EID_{50}/ml) were used either undiluted or diluted 1:2 in beef-heart infusion broth (Difco) and, unless otherwise indicated, the duration of aerosol exposure was 5 minutes. The calculated maximum inhaled dose was $10^{6.6}$ to $10^{7.3}$ EID_{50}. Suspensions of the AD strain of C. burnetii used in generating the aerosols consisted of 1:10 dilutions of 10% chick embryo yolk sacs that contained $10^{5.2}$ to $10^{5.6}$ $YSLD_{50}$/ml. Five-minute aerosol exposures to C. burnetii were made in a modified Henderson apparatus as described by Roessler and Kautter.[2] The calculated maximum inhaled dose was approximately 6 to 14 $YSLD_{50}$.

In the initial studies, guinea pigs were exposed to aerosols of C. burnetii 24 hours after exposure to influenza virus. The combined results of several experiments are shown in Table 1, Experiment A. Previous exposure to influenza virus apparently enhanced the ability of guinea pigs to survive subsequent challenge with a lethal dose of C. burnetii. Table 1, Experiment B, shows the results obtained when intervals other than 24 hours were used between exposures. Evidence of interference with C. burnetii was observed up to 4 days following exposure to influenza virus. Similar results were obtained when the exposure time to influenza virus was increased from 5 minutes to 30 minutes, although a few more deaths due to influenza virus alone occurred. Deaths caused by influenza were easily discernible from deaths caused by C. burnetii because the influenza mortality occurred before the 3rd day, and deaths due to the rickettsiae occurred after the 7th day. There was no significant difference in the time of death of guinea pigs following combined exposure as compared with those following exposure to C. burnetii 24 hours or more before exposure to influenza virus.

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* In conducting the research reported here, the investigators adhered to "Principles of Laboratory Animal Care" as established by the National Society for Medical Research.

1. Janssen, R.J., W.A. Chappell, and P.J. Gerone. 1963. Synergistic activity between PR8 influenza virus and Staphylococcus aureus in the guinea pig. Amer. J. Hyg. 78:275-284.

2. Roessler, W.G., and D.A. Kautter. 1962. Modifications to the Henderson apparatus for studying air-borne infections: Evaluations using aerosols of Listeria monocytogenes. J. Infect. Dis. 110:17-22.

The mechanism of this interference, and whether or not an interferon-like substance may be involved, has not been determined. The phenomenon is apparently not caused by an interference of influenza virus with the ability of C. burnetii to infect the guinea pig. This is based on the fact that the guinea pigs exposed to both organisms developed a complement-fixing antibody to C. burnetii comparable in titer to the antibody levels of the guinea pigs surviving exposure to C. burnetii alone. These animals also elicited similar febrile responses (104 to 105 F) and gross pathology when compared with singly infected guinea pigs sacrificed at the same intervals.

TABLE 1. INTERFERENCE OF C. BURNETII, STRAIN AD, BY INFLUENZA VIRUS, PR8 STRAIN, IN GUINEA PIGS

Experiment	Aerosol Inocula		Days Between Exposures	Mortality Ratio, dead/exposed
	First Exposure	Second Exposure		
A	PR8 virus	-	-	2/28
	-	C. burnetii	-	21/28
	PR8 virus	C. burnetii	1	4/28
B	PR8 virus	C. burnetii	0	0/4
	PR8 virus	C. burnetii	1	0/4
	PR8 virus	C. burnetii	2	0/4
	PR8 virus	C. burnetii	3	0/4
	PR8 virus	C. burnetii	4	1/4
	PR8 virus	C. burnetii	5	3/4
	PR8 virus	C. burnetii	6	2/4
	PR8 virus	C. burnetii	7	3/4
	PR8 virus	-	-	0/4
	-	C. burnetii	-	3/4
	NCAF[a]	C. burnetii	-	2/4

a. Normal chorioallantoic fluid.

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